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# Intrapair Comparison of Life-Course Appetite and Physical Activity in Elderly Danish Twins: Reliability and Association With Subsequent Survival

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Avoiding overeating and being physically active is associated with healthy aging, but methodological issues challenge the quantification of the association. Intrapair comparison of twins is a study design that attempts to minimize social norm-driven biased self-reporting of lifestyle factors. We aimed to investigate the association between self-reported lifestyle factors and subsequent survival in 347 Danish twin pairs aged 70 years and older and, additionally, to investigate the reliability of these self-reports. The twins were interviewed in 2003 and followed for mortality until 2015. They were asked to compare their appetite and physical activity to that of their co-twins in different stages of life. On an individual level, we found a positive association between current self-reported physical activity and late-life survival for elderly twins. This was supported by the intrapair analyses, which revealed a positive association between midlife and current physical activity and late-life survival. A positive association between lower appetite and late-life survival was found generally over the life course in the individual level analyses but not in the intrapair analyses. Kappa values for the inter-twin agreement on who ate the most were 0.16 to 0.34 in different life stages, and for physical activity 0.19 to 0.26, corresponding to a slight-to-fair agreement. Approximately, 50% of the twin pairs were not in agreement regarding physical activity, and of these twins 75% (95% CI: 67–82%) considered themselves the most active twin. These findings indicate a still-existing tendency of answering according to social norms, even in a twin study designed to minimize this.

■ **Keywords:** physical activity, appetite, self-report, elderly, twins, reliability, survival

Avoiding overeating and being physically active have in numerous studies been documented as two lifestyle factors that improve multiple parameters of healthy aging (Beydoun et al., 2014; Kujala, 2011; Loef & Walach, 2012; Warburton et al., 2006). Conversely, a high-calorie diet without exercise increases the risk of cardiovascular disease and diabetes (Chen et al., 2015; Orozco et al., 2008), and furthermore, suppresses specific longevity genes that are active in the cellular defense against aging and age-related diseases (North & Sinclair, 2012). Reviews of the association between physical activity and overall mortality of elderly persons typically report on studies showing a decrease in mortality of up to 40% when comparing physically active elderly persons to elderly persons with a more sedentary lifestyle (Rizutto & Fratiglioni, 2014; Taylor, 2014;

Vogel et al., 2009). The J- or U-shaped association between Body Mass Index (BMI) and mortality is similarly well established for middle-aged and younger elderly persons (Bray, 1987; Gonzalez et al., 2010), although decreasingly U-shaped with advancing age for the age range 70–95 years (Thinggaard et al., 2010). The association between overeating and mortality is far less studied. This may be due to the complexity of such a study, as it is difficult to measure

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overeating. Moreover, the association may be influenced by numerous variables; for example, physical activity and stress (Torres & Nowson, 2007; Westerterp, 2010). Furthermore, methodological issues have challenged the quantification of the degree to which avoiding overeating and being physically active increases the chances of a long and healthy life. Traditionally, the quantification of the exposure has been based on self-reported food intake and physical activity. More recently, several direct measurements of food intake and physical activity have provided more accurate measures, such as urinary nitrogen, doubly labeled water, accelerometers, pedometers, and multisensor armbands (Kowalski et al., 2012; Park et al., 2014). However, most of these studies were smaller and with shorter follow-up compared to studies with self-reported measurements of food intake and/or physical activity. Studies based on self-reports are likely to be biased toward a healthier lifestyle, and the associations may be underestimated if those with the unhealthiest lifestyle have the most biased reporting (Pietiläinen et al., 2010).

Here, we report on a 12-year follow-up study of mortality among middle-aged and elderly twins who answered questions on intrapair differences in appetite and physical activity in childhood, adolescence, midlife, and at intake of the study. The aim was to test whether there was an association between intrapair differences regarding appetite and/or physical activity and subsequent survival.

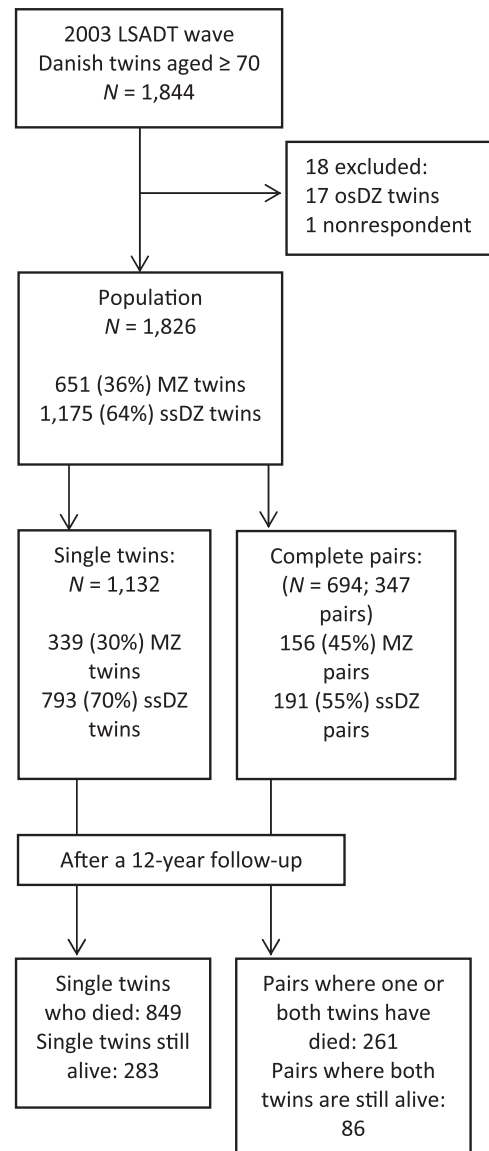
This intrapair comparison design provides an opportunity to account for unobserved familial confounding, exploiting the fact that twins share their childhood environment and are matched partly (same-sex dizygotic [ssDZ] twins) or fully (monozygotic [MZ] twins) on genetic makeup. Hence, intrapair comparisons of exposure-discordant twin pairs will per design be controlling for these familial factors (McGue et al., 2010). When reporting on eating behavior and physical activity, twin studies are considered more accurate, since the tendency to answer according to social norms is diminished when the twins compare themselves to one another (Bogl et al., 2009). By comparing the co-twins' responses, we assessed the degree of misreporting in self-reported current and previous lifestyle habits.

Thus, the aim of this study was to investigate whether life-course appetite and physical activity were associated with late-life survival when familial factors were controlled for; and, additionally, to investigate the reliability of self-reports regarding appetite and physical activity in an intrapair twin comparison study.

## Materials and Methods

### Study Population

The population under study consisted of 1,826 same-sex twins of more than 70 years of age participating in the 2003 wave of the Longitudinal Study of Aging Danish Twins



**FIGURE 1**

**Study population.** Note: MZ = monozygotic; osDZ = opposite-sex dizygotic; ssDZ = same-sex dizygotic.

(LSADT), a subsample from the Danish Twin Registry (Skytthe et al., 2002; 2006). Figure 1 illustrates the selection process of the study population.

The LSADT began in 1995 with an assessment of same-sex twin pairs born in Denmark prior to 1920. The initial cohort was followed up every second year until 2005, including sequential assessments of participants who had aged into the catchment age range, and additional cohorts were added in 1997, 1999, and 2001. This study used the LSADT wave from 2003, since this was the only year the twins were asked to compare their appetite and physical activity to that of their co-twin. The survey also included twins whose co-twin had died or declined to participate,

and the survey had a participation rate of 82% (McGue & Christensen, 2007). Participants were interviewed face to face in their home by trained interviewers. If both twins participated, the co-twins were interviewed by different interviewers to minimize interviewer bias.

## Measures

**Co-twin comparison of lifestyle factors.** In the face-to-face interview, the twins were asked individually to relate themselves to their co-twin when comparing their appetite and physical activity at four different stages of life: childhood, adolescence, middle age, and at intake of the study. They did so by answering the questions: 'Who ate the most?' and 'Who was most physically active?' Their response alternatives were 'Me', 'My twin', 'Equally', and 'Don't know' (and missing if the co-twin was dead at that life stage).

**Survival.** Survival time was gathered from interview date and until follow-up was terminated by either death, emigration, or end of follow-up in March 2015, whichever came first. No subjects were lost to follow-up and no emigration occurred in the study period. Information on survival status was acquired through the Central Person Registry by the use of a unique personal identification number available to all persons with permanent residence in Denmark (Thygesen & Ersbøll, 2011).

**Cognition.** Cognitive functioning was based on five brief cognitive tests, which were sensitive to age-related changes in cognition: (1) a category fluency task in which the participant was asked to name as many animals as possible in 1 minute, (2) forward and (3) backward digit span, and (4) immediate and (5) delayed recall of a 12-item list. The overall composite measure of cognitive functioning was computed by adding the sum of the five standardized measures using means and standard derivations from the initial LSADT assessment in 1995 (McGue & Christensen 2001; 2002).

**Smoking status.** The twins were asked about their smoking behavior. They were categorized as a non-smoker, former smoker, or current smoker.

**Body Mass Index (BMI).** Height in meters and weight in kilograms were self-reported and were used to calculate BMI ( $\text{weight/height}^2$ ).

## Data Analysis

### Individual Level Survival Analysis

On an individual level, the association between appetite and physical activity and subsequent survival was analyzed using Cox regression models. The estimates for risk of death was given by comparing twins who answered 'My co-twin ate most' or 'My co-twin was most physically active' to their respective reference groups 'I ate most' and 'I was most

physically active'. Twins who answered 'Equally' or 'Don't know' were not included in these analyses as the purpose was to compare the mortality risk when answering 'Me' versus answering 'My twin' when asked about appetite and physical activity. As the data partly pertained to twin pairs, and because observation within twin pairs might be correlated, the analyses were performed using the robust estimator of variance, assuming independence between pairs. The proportional-hazards assumption was tested using Schoenfeld residuals.

Four different Cox regression models were used to calculate the hazard ratio (HR) and 95% confidence interval (CI) for mortality risk. In models 1 and 2, appetite and physical activity were analyzed separately, and in models 3 and 4, both lifestyle factors were included in the same regression. Furthermore, models 1 and 3 were adjusted for age and sex, and models 2 and 4 were additionally adjusted for known risk factors for mortality in late life: cognition, smoking status, and BMI. Cognition was a continuous variable; smoking status was categorized into non-smoker, former smoker, and current smoker; and BMI was categorized into the following groups: <18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9,  $\geq 35.0$ .

### Intrapair Survival Analysis

In complete twin pairs, the twins served as each other's control person regarding answers on the lifestyle factors appetite and physical activity. Intrapair analyses were performed on pairs discordant for these lifestyle factors, which enabled us to examine their association with late-life survival. Only pairs in which one or both twins had died were used in the intrapair analysis.

The hypothesis regarding the association between appetite and survival was that the twin who ate more lived a shorter life. Regarding physical activity, the hypothesis was that the twin who was more physically active lived longer. The association between appetite and physical activity and subsequent survival was examined, using the binomial distribution, by investigating the proportion of complete twin pairs that fulfilled the aforementioned hypotheses.

### Reliability Analysis

The reliability of the twins' answers regarding appetite and physical activity was analyzed by creating a three-by-three intertwin agreement matrix of the categorical variables, as depicted in Figure 2. There were three levels of agreement: 'Agreement', 'Partly agreement', and 'Disagreement'. 'Agreement' included twins who were of the same opinion regarding who ate the most or who was most physically active at a given life stage. If one twin answered 'Equally' and the other answered 'Me' or 'My twin', the twins were categorized as being in 'Partly agreement'. 'Disagreement' included twins who had completely opposite views on who ate the most or who was most physically active.

		Twin 2's answer:		
		Twin 1	Equally	Twin 2
Twin 1's answer:	Twin 1	<b>A</b> (Agreement)	<b>B</b> (Partly agreement)	<b>C</b> (Disagreement)
	Equally	<b>D</b> (Partly agreement)	<b>E</b> (Agreement)	<b>F</b> (Partly agreement)
	Twin 2	<b>G</b> (Disagreement)	<b>H</b> (Partly agreement)	<b>I</b> (Agreement)

**FIGURE 2**

(Colour online) Description of the level of agreement between the twins' answers as to 'Who ate most?' and 'Who was most physically active?'.

Cohen's kappa value ( $\kappa$ ) was used as a measurement of intertwin agreement. A  $\kappa$  value of less than 0.0 was interpreted as poor agreement, 0.00–0.20 indicated slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and more than 0.81 interpreted as almost perfect agreement (Landis & Koch, 1977).

A subanalysis was performed by calculating a weighted kappa, where a weight of 0.5 was given to answers categorized as partly agreement in order to mathematically distinguish those pairs from pairs in disagreement, as it could be argued that twins in partly agreement were closer to an agreement.

Of the twins in the categories partly agreement and disagreement, we also investigated whether there was a tendency for the twins to modify their answers toward a healthier lifestyle; for example, considering themselves to be eating less and/or being more physically active compared to their co-twin.

All statistical analyses were performed using Stata 13.1 (Stata Corporation, College Station, TX).

## Results

Of the 1,826 twins in the study, 347 were complete pairs who were included in the intrapair analyses. The rest of the study population were single twins ( $N = 1,132$ ) who, together with the individuals from the complete pairs, were included in the individual-level analyses.

The study population consisted of 809 (44%) males and 1,017 (56%) females, whereas the zygosity distribution was 651 (36%) MZ twins and 1,175 (64%) ssDZ twins. When we examined only complete pairs, the distributions were 147 (42%) male pairs and 200 (58%) female pairs, and when we divided the pairs into zygosity, the numbers were: 156 (45%) MZ pairs and 191 (55%) ssDZ pairs (Figure 1 and Table 1). Complete twin pairs were younger than the total study population, which explains the higher cognitive score (McGue & Christensen, 2001).

Of the 1,132 single twins, 849 (75%) twins had died after the 12-year follow-up. A similar percentage was found in the 347 complete twin pairs with 261 (75%) pairs where one or both twins had died after the follow-up.

## Individual-Level Survival Analysis

We found an association between appetite and late-life survival in adolescence (HR: 0.81, 95% CI: 0.67–0.99) in model 1, where we adjusted for age and sex (Table 2). If further adjusted for known risk factors (cognition, smoking status, and BMI), an association was found in childhood (HR: 0.79, 95% CI: 0.65–0.97) and adolescence (HR: 0.79, 95% CI: 0.63–0.98) as seen in model 2, which showed a statistically significantly lower mortality risk for the twin who ate less.

In both model 3 (HR: 0.77, 95% CI: 0.60–0.99) and model 4 (HR: 0.73, 95% CI: 0.56–0.96), an association between middle-age appetite and late-life survival was found. All HRs in childhood, adolescence, and middle-age were less than 1, indicating that eating less might be a protective factor on the mortality risk, although not statistically significant.

We did find a statistically significant association between physical activity at intake of the study and late-life survival for elderly twins, indicating an increase in mortality risk for the less active twin (HR: 2.12, 95% CI: 1.52–2.95) when adjusting for age, sex, cognition, smoking status, and BMI. The association was statistically significant for all four Cox regression models. As an example, Table 3 shows the fully adjusted model 4 with physical activity and appetite at intake of the study, including all risk factors. These adjustments showed the expected pattern of low physical activity, older age, lower cognitive status, and both high and low BMI being associated with poorer survival in late life. If BMI was excluded from the analyses, the proportional hazards assumption was fulfilled, and it did not alter the estimates (results not shown).

Furthermore, we compared the group of twins who answered 'I ate the most' to the group who answered 'My twin



**TABLE 1**

**Descriptive Characteristics for All Twins in the Study Population (N = 1,826) and for Complete Twin Pairs (N = 694) Listed by Sex**

Study population N individuals (%)	Male 809 (44)		Female 1,017 (56)	
	N	Mean [95% CI]	N	Mean [95% CI]
Age	809	78.6 [78.2–78.9]	1,017	80.1 [79.8–80.5]
Age at death	586	85.1 [84.6–85.5]	676	87.9 [87.4–88.3]
Height	806	172.3 [171.9–172.8]	1,013	161.5 [161.1–161.9]
Weight	806	74.9 [74.2–75.7]	1,004	62.7 [61.9–63.4]
BMI	806	25.2 [24.9–25.4]	999	23.9 [23.7–24.2]
Cognition	749	1.8 [1.5–2.0]	928	1.7 [1.5–2.0]
Complete pairs N Individuals (%)	Male 294 (42)		Female 400 (58)	
	N	Mean [95% CI]	N	Mean [95% CI]
Age	294	76.9 [76.4–77.4]	400	77.9 [77.5–78.3]
Age at death	188	84.5 [83.8–85.2]	225	86.0 [85.3–86.7]
Height	293	172.8 [172.1–173.5]	399	161.9 [161.3–162.5]
Weight	293	74.8 [73.6–76.0]	396	63.2 [62.1–64.4]
BMI	293	24.0 [24.7–25.3]	396	24.0 [23.6–24.4]
Cognition	281	2.5 [2.0–2.9]	376	2.6 [2.2–2.9]

Note: Population sizes differ due to missing data.

**TABLE 2**

**Hazard Ratios (HR) for Mortality Risk Associated With Appetite and Physical Activity for Different Stages of Life**

	Cox regressions							
	N	Model 1 <sup>a</sup> HR [95% CI]	N	Model 2 <sup>b</sup> HR [95% CI]	N	Model 3 <sup>a</sup> HR [95% CI]	N	Model 4 <sup>b</sup> HR [95% CI]
Childhood								
Appetite	674	0.85 [0.70–1.02]	628	0.79 [0.65–0.97] <sup>c,d</sup>	425	0.88 [0.69–1.10]	396	0.85 [0.67–1.09]
Activity	830	0.94 [0.79–1.12]	764	0.90 [0.75–1.08]		0.95 [0.73–1.23]		0.82 [0.62–1.08]
Adolescence								
Appetite	596	0.81 [0.67–0.99] <sup>d</sup>	551	0.79 [0.63–0.98] <sup>c,d</sup>	365	0.80 [0.62–1.03]	338	0.81 [0.61–1.06] <sup>c</sup>
activity	816	1.03 [0.87–1.23] <sup>c</sup>	745	1.01 [0.83–1.22]		1.24 [0.95–1.61]		1.11 [0.83–1.51] <sup>c</sup>
Middle-age								
Appetite	605	0.88 [0.72–1.07]	554	0.81 [0.66–1.01] <sup>c</sup>	401	0.77 [0.60–0.99] <sup>d</sup>	367	0.73 [0.56–0.95] <sup>d</sup>
Activity	842	1.13 [0.94–1.36]	770	1.09 [0.88–1.35]		1.25 [0.93–1.68]		1.11 [0.79–1.56]
Intake								
Appetite	415	1.23 [0.96–1.58]	389	1.09 [0.82–1.44]	310	0.95 [0.71–1.27]	290	0.87 [0.63–1.20] <sup>c</sup>
activity	568	1.79 [1.44–2.23] <sup>e</sup>	533	1.69 [1.34–2.13] <sup>c,e</sup>		2.17 [1.61–2.93] <sup>e</sup>		2.12 [1.52–2.95] <sup>c,e</sup>

Note: Appetite and activity estimates are risk of death if twin answered 'My co-twin ate most/my co-twin was most physically active' compared to the reference group 'I ate most/I was most active'. All analyses are on an individual level. In model 1 and 2, appetite and physical activity were analyzed separately, and in model 3 and 4, both lifestyle factors were included in the same regression. Population sizes differ due to missing data and exclusion of the answers 'Equally' and 'Don't know'.

<sup>a</sup>Adjusted for age and sex; <sup>b</sup>Adjusted for age, sex, cognition, smoking status, and BMI; <sup>c</sup>Proportional hazards assumption is violated; <sup>d</sup>p values < .05;

<sup>e</sup>p values < .001.

ate the most' using a *t* test. We found a statistically significantly higher BMI in the group that considered themselves as eating most in all four stages of life. No statistically significant difference in BMI was found when comparing the two groups who answered 'I was most active' and 'My twin was most active' (results not shown).

### Intrapair Survival Analysis

We examined the intrapair association between appetite and physical activity and subsequent survival for twins who were in agreement, partly agreement, and both combined. The associations between appetite and late-life survival found in the individual-level survival analysis were not supported by the intrapair analyses.

There was an indication that eating more at intake of the study might be a protective factor on survival for elderly

twins, although the observed tendency was not statistically significant. This can be seen in Table 4A which shows that twin pairs who confirmed the hypothesis, meaning where the twin who ate less lived longer, comprised a little more than 50% in childhood, adolescence, and middle age, and a little less than 50% at intake of the study.

A statistically significant association was found between midlife and physical activity at intake of the study and late-life survival with 61% (95% CI: 53–70%) and 74% (95% CI: 67–81%), respectively (Table 4B), as also suggested by the individual level analyses.

### Reliability Analysis

The proportion of twin pairs in agreement about their appetite were between 52% and 62% ( $\kappa$ : 0.16 to 0.34) for different stages of life. For physical activity, the agreement

**TABLE 3**

**Hazard Ratios for Mortality Risk Associated With Appetite and Physical Activity on an Individual Level at Intake of the Study Adjusted for Age, Sex, Cognition, Smoking Status, and BMI**

At intake N = 290	HR [95% CI]
<b>Appetite</b>	
I ate most	1.00
Co-twin ate most	0.87 [0.63–1.20]
<b>Activity</b>	
I was most active	1.00
Co-twin most active	2.12 [1.52–2.95]
<b>Age</b>	1.08 [1.04–1.12]
<b>Sex</b>	
Male	1.00
Female	0.88 [0.63–1.23]
<b>Cognition</b>	0.91 [0.87–0.95]
<b>Smoking status</b>	
Non-smoker	1.00
Current	1.17 [0.75–1.83]
Former	1.17 [0.82–1.66]
<b>BMI</b>	
<18.5	1.98 [1.14–3.44]
18.5–24.9	1.00
25.0–29.9	0.98 [0.69–1.40]
30.0–34.9	0.90 [0.40–2.04]
≥35.0	2.19 [1.09–4.41]

Note: Proportional-hazards assumption is violated in this multivariate Cox regression analysis. If excluding BMI adjustments, the proportional-hazards assumption was fulfilled, and did not alter the conclusion.

**TABLE 4A**

**Intrapair Analysis of the Association Between Appetite and Survival**

	Pairs discordant for appetite* N	Pairs where one or both twins have died N	Pairs confirming the hypothesis** N [%, 95% CI]
<b>Appetite</b>			
<b>Childhood</b>			
Agreement	54	38	24 [63, 46–78]
Partly agreement	89	71	38 [54, 41–65]
Total	143	109	62 [57, 47–66]
<b>Adolescence</b>			
Agreement	34	25	14 [56, 35–76]
Partly agreement	91	68	40 [59, 46–71]
Total	125	93	54 [58, 47–68]
<b>Middle age</b>			
Agreement	36	26	15 [58, 37–77]
Partly agreement	103	77	39 [51, 39–62]
Total	139	103	54 [52, 42–62]
<b>At intake</b>			
Agreement	53	45	24 [53, 38–68]
Partly agreement	94	71	30 [42, 31–55]
Total	147	116	54 [47, 37–56]

Note: \*Excluding pairs where answers are in disagreement and answers were both twins answered 'Equally', equivalent to quadrants C, E, and G in Figure 2.

\*\*The hypothesis for appetite is that the twin who ate more lived shorter and vice versa; the twin who ate less lived longer.

percentages were between 47% and 57% ( $\kappa$ : 0.19 to 0.26), corresponding to slight-to-fair agreement on answers regarding both appetite and physical activity. Using the weighted kappa increased the kappa values with 0.02 to 0.06, which made no difference to the interpretation. The proportion of twin pairs in agreement, partly agreement,

**TABLE 4B**

**Intrapair Analysis of the Association Between Physical Activity and Survival**

Physical Activity	Pairs discordant for physical activity* N	Pairs where one or both twins have died N	Pairs confirming the hypothesis** N [%, 95% CI]
<b>Childhood</b>			
Agreement	57	43	23 [53, 38–69]
Partly agreement	122	88	50 [57, 46–67]
Total	179	131	73 [56, 47–64]
<b>Adolescence</b>			
Agreement	45	33	16 [48, 31–66]
Partly agreement	129	98	58 [59, 49–69]
Total	174	131	74 [56, 48–65]
<b>Middle age</b>			
Agreement	61	46	27 [59, 43–73]
Partly agreement	132	94	59 [63, 52–73] <sup>a</sup>
Total	193	140	86 [61, 53–70] <sup>a</sup>
<b>At intake</b>			
Agreement	86	72	55 [76, 65–86] <sup>a</sup>
Partly agreement	132	93	67 [72, 62–81] <sup>a</sup>
Total	218	165	122 [74, 67–80] <sup>a</sup>

Note: \*Excluding pairs where answers are in disagreement and answers were both twins answered 'Equally', equivalent to quadrants C, E, and G in Figure 2.

\*\*The hypothesis for physical activity is that the twin who was less physically active lived shorter and vice versa, the twin who was more physically active lived longer.

<sup>a</sup>p value < .05.

and disagreement, as well as the kappa values are shown in Table 5.

Complete twin pairs where one or both twins had answered 'Don't know' were included in the kappa intertwin agreement calculation as 'Equally' in a subanalysis, since it could be argued that those two answers were similar. However, it did not alter the kappa values (results not shown).

As shown in Table 6, a clear tendency for the twins to regard themselves as the most physically active was found in twin pairs who did not agree on their answers, that is, in partly agreement, disagreement, or both combined. The percentages of twins considering themselves the most active were between 73% (95% CI: 64–80) and 90% (95% CI: 73–98) for different life stages. If the twins were in complete disagreement, it was because nearly all of them considered themselves the most active, and in the combined group of complete and partly disagreement, three out of four twins answered 'Myself' to the question 'Who was most active?' (75%, 95% CI: 67–82).

## Discussion

When investigating the intertwin agreement, we found a slight-to-fair agreement between the twins regarding their answers on appetite and physical activity in childhood, adolescence, middle age, and at intake of the study. A clear tendency for the twins to consider themselves the most physically active was observed in twins who were not in agreement. With three out of four twins answering 'Myself' to the question 'Who was most active?', an overestimation

**TABLE 5**  
Intrapair Reliability of Answers Regarding Appetite and Physical Activity

	Pairs N	Agreement %	Partly agreement %	Disagreement %	Kappa	Agreement weight 0.5 % <sup>a</sup>	Kappa weight 0.5
Appetite							
Childhood	251	62	35	3	0.34	79	0.38
Adolescence	233	59	39	2	0.22	78	0.27
Middle age	234	52	44	4	0.16	74	0.21
At intake	243	54	39	7	0.25	73	0.27
Activity							
Childhood	323	57	37	6	0.26	76	0.28
Adolescence	318	53	41	6	0.19	73	0.21
Middle age	305	50	44	6	0.21	72	0.26
At intake	306	47	43	10	0.22	69	0.28

Note: <sup>a</sup>agreement + ½ \*partly agreement. For description of agreement, partly agreement and disagreement see Figure 2. Agreement corresponds to quadrants A, E, and I, Partly agreement corresponds to quadrants B, D, F, and H, and Disagreement corresponds to quadrants C and G. N does not include pairs where one or both twins answered 'Don't know'.

**TABLE 6**  
Description of Twins not in Agreement in Their Intrapair Comparison in Different Life Stages

	Partly agreement			Disagreement			Total		
	Pairs	Answered 'Myself'		Pairs	Answered 'Myself'		Pairs	Answered 'Myself'	
	N	%	[95% CI]	N	%	[95% CI]	N	%	[95% CI]
Appetite									
Childhood	89	53	[42–63]	7	57	[18–90]	96	53	[43–63]
Adolescence	91	46	[36–57]	5	60	[15–95]	96	47	[37–57]
Middle age	103	51	[40–60]	9	44	[14–79]	112	50	[40–60]
At intake	94	48	[37–58]	18	33	[13–59]	112	46	[36–55]
Activity									
Childhood	122	74	[65–81]	18	83	[59–96]	140	75	[67–82]
Adolescence	129	73	[64–80]	20	90	[68–99]	149	75	[67–82]
Middle age	132	76	[68–83]	19	74	[49–91]	151	76	[68–82]
At intake	132	74	[66–81]	30	90	[73–98]	162	77	[70–83]

Note: For description of partly agreement and disagreement, see Figure 2. Partly agreement corresponds to quadrants B, D, F, and H and disagreement corresponds to quadrants C and G.

of physical activity toward a healthier lifestyle was indicated (Adams et al., 2005). The twin study design was designed to minimize the tendency of answering according to social norms when participants were asked about lifestyle factors (Bogl et al., 2009), but as the present study showed, this tendency was not eliminated.

Previous studies strongly supported an inverse association between physical activity and all-cause mortality (Physical Activity Guidelines Advisory Committee, 2008). As expected, the present study found a positive association between physical activity at intake of the study and late-life survival in elderly Danish twins, when important covariables were controlled for. Previous reviews have shown a lower mortality risk for the most active elderly (Rizutto & Fratiglioni, 2014; Taylor, 2014; Vogel et al., 2009). Our study hereby supports the existing studies suggesting that the most active tend to live longer, also when familial factors are controlled for.

In adolescence and middle age, physical activity seemed to be a protective factor for late-life survival for the most physically active twin with HRs greater than 1, although not statistically significant. A tendency for the mortality risk to increase throughout life was observed for the less active twin, which was supported by the intrapair analyses.

This tendency was not found in intrapair comparisons in a previous study of twins in adulthood, which only found a statistically non-significant lower risk of death, although not statistically significant, for the twin engaged in persistent vigorous physical activity (HR 0.72, 95% CI: 0.48–1.07) compared to the non-persistent vigorously physically active twin, when controlling for covariates (Karvinen et al., 2015). Additionally, more misclassification in the reporting of lifestyle factors in early life could be the basis for the observed tendency toward increasing mortality risk through life for the less active twin. It is also likely that the association found was confounded by one twin having a known or unknown disease at intake of the study, which could influence both discordance of physical activity within the twin pair and late-life survival.

High and low BMI at intake of the study was associated with higher mortality. We found no alteration in the overall conclusion when including and excluding BMI as a covariate in the survival analyses. Hence, it seems unlikely that collinearity between appetite and BMI should have influenced the results. Furthermore, BMI was statistically significantly higher for twins who considered themselves as eating the most compared to the twins who considered their co-twin as eating the most on an individual level in all four



stages of life. This indicated that the answers regarding appetite were reliable. On the individual level, an association between appetite over the life course and late-life survival was found, but in the intrapair analyses, which controls for genetic factor (full or partly) and shared early life environment, no association was found. The lack of an association could be due to measurement error of appetite and/or lack of statistical power. However, the sample size was large enough to be able to demonstrate an association between midlife and physical activity and survival also in the intrapair analyses.

We found that 33% to 66% of the twins considered themselves to be eating most when examining whether a tendency of answering according to social norms existed for twins not in agreement. There was a slight tendency for twins who disagreed on their appetite in middle age and at intake of the study to consider their co-twin as eating more, but the population number in this group was too small for the result to be conclusive.

Information on appetite and physical activity is collected retrospectively (except at intake of the study), which makes recall bias a possibility. However, the study design seeks to minimize the influence of both social norm-driven bias as well as recall bias by comparing twins' answers on an intrapair level and by getting the information from two individuals.

Some other limitations of this study must be noted. On an individual level, 806 of the 1,826 participants could not answer the questions of co-twin difference in appetite and physical activity at intake since their co-twin had died. Only complete pairs where one or both twins had died were useful in the intrapair analyses when investigating the influence of appetite and physical activity on late-life survival. This reduced the study population by approximately 25%. However, the results from our individual analyses, showing an increase in mortality throughout life for the less active twin, were supported by the results from the intrapair analyses.

Another concern could be that twins differ from the background population, but previous research has repeatedly shown that twins are similar to the background population regarding adult mortality and major causes of death, except suicide, for which twins have a lower risk (Öberg et al., 2012; Christensen & McGue, 2008; Christensen et al., 1995; Tomassini et al., 2003).

The strengths of this study include complete follow-up on mortality, as national population registers were used. Twin-pair comparisons provided a unique opportunity to examine the association between appetite and physical activity on late-life survival, allowing the twins to function as each other's control persons. By comparing twin responses on lifestyle factors, we were not only able to examine late-life survival, but also to categorize the twins' answers according to level of agreement and thereby investigating the reliability of their answers.

Our study indicates social norm-driven biased reporting of life style — even in a study designed to minimize this tendency. The bias can lead to an overestimation of the effect size of continuous exposures if the misreporting corresponds to those with the most extreme values misreporting the most. For binary exposures, social norm-driven biased reporting will tend to underestimate the effect as the unexposed group will be 'diluted' with individuals who are actually exposed to the harmful factor.

In conclusion, late-life physical activity is associated with better survival even when familial factors are controlled for. However, the reliability of self-reports on lifestyle factors, even in designs made to minimize social norm-driven reporting bias, is low and it seems that elderly Danish twins tend to romanticize their own performance when comparing themselves to each other.

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## References

- Adams, S. A., Matthews, C. E., Ebbeling, C. B., Moore, C. G., Cunningham, J. E., Fulton, J., & Herbert, J. R. (2005). The effect of social desirability and social approval on self-reports of physical activity. *American Journal of Epidemiology*, 161, 389–398.
- Beydoun, M. A., Beydoun, H. A., Gamaldo, A. A., Teel, A., Zonderman, A. B., & Wang, Y. (2014). Epidemiologic studies of modifiable factors associated with cognition and dementia: Systematic review and meta-analysis. *BioMed Central Public Health*, 14, 643.
- Bogl, L. H., Pietiläinen, K. H., Rissanen, A., & Kaprio, J. (2009). Improving the accuracy of self-reports on diet and physical exercise: The co-twin control method. *Twin Research and Human Genetics*, 12, 531–540.
- Bray, G. A. (1987). Overweight is risking fate. Definition, classification, prevalence, and risks. *Human Obesity*, 499, 14–28.
- Chen, L., Pei, J. H. P., Kuang, J., Chen, H. M., Chen, Z., Li, Z. W., & Yang, H. Z. (2015). Effect of lifestyle intervention in patients with type 2 diabetes: A meta-analysis. *Metabolism — Clinical and Experimental*, 64, 338–347.
- Christensen, K., & McGue, M. (2008). Academic achievements in twins. *British Medical Journal*, 337, a651.
- Christensen, K., Vaupel, J. W., Holm, N. V., & Yashin, A. I. (1995). Mortality among twins after age 6: Fetal origins hypothesis versus twin method. *British Medical Journal*, 310, 432–436.
- Gonzalez, A. B., Hartge, P., Cerhan, J. R., Flint, A. J., Hannan, L., MacInnis, R. J., ... Thun, M. J. (2010). Body mass index

- and mortality among 1.46 million white adults. *New England Journal of Medicine*, 363, 2211–2219.
- Karvinen, S., Waller, K., Silvennoinen, M., Koch, L. G., Britton, S. L., Kaprio, J., ... Kujala, U. M. (2015). Physical activity in adulthood: Genes and mortality. *Scientific Reports*, 5, Article no. 18259.
- Kowalski, K., Rhodes, R., Naylor, P. J., Tuokko, H., & MacDonald, S. (2012). Direct and indirect measurement of physical activity in older adults: A systematic review of the literature. *International Journal of Behavioral Nutrition and Physical Activity*, 9, 148.
- Kujala, U. M. (2011). Physical activity, genes, and lifetime predisposition to chronic disease. *European Review of Aging and Physical Activity*, 8, 31–36.
- Landis, J. R., & Koch, C. G. (1977). The measurement of observer agreement for categorical data. *Biometrics*, 33, 159–174.
- Loef, M., & Walach, H. (2012). The combined effects of healthy lifestyle behaviours on all cause mortality: A systematic review and meta-analysis. *Preventive Medicine*, 55, 163–170.
- McGue, M., & Christensen, K. (2001). The heritability of cognitive functioning in very old adults: Evidence from Danish twins aged 75 years and older. *Psychology and Aging*, 16, 272–280.
- McGue, M., & Christensen, K. (2002). The heritability of level and rate-of-change in cognitive functioning in Danish twins aged 70 years and older. *Experimental Aging Research*, 28, 435–451.
- McGue, M., & Christensen, K. (2007). Social activity and healthy aging: A study of aging Danish twins. *Twin Research and Human Genetics*, 10, 255–265.
- McGue, M., Osler, M., & Christensen, K. (2010). Causal inference and observational research: The utility of twins. *Perspectives on Psychological Science*, 5, 546–556.
- North, B. J., & Sinclair, D. A. (2012). The intersection between aging and cardiovascular disease. *Circulation Research*, 110, 1097–1108.
- Öberg, S., Cnattingius, S., Sandin, S., Lichtenstein, P., Morley, R., & Iliadou, A. N. (2012). Twinship influence on morbidity and mortality across lifespan. *International Journal of Epidemiology*, 41, 1002–1009.
- Orozco, L. J., Buchleitner, A. M., Gimenez-Perez, G., Roqué I Figuls, M., Richter, B., & Mauricio, D. (2008). Exercise or exercise and diet for preventing type 2 diabetes mellitus (Review). *Cochrane Database of Systematic Reviews*, 3, 1–85.
- Park, J., Kazuko, I. T., Kim, E., Kim, J., & Yoon, J. (2014). Estimating free-living human energy expenditure: Practical aspects of the doubly labeled water method and its applications. *Nutrition Research and Practice*, 8, 241–248.
- Physical Activity Guidelines Advisory Committee. (2008). Physical Activity Guidelines Advisory Committee report. Washington, DC: Department of Health and Human Services.
- Pietiläinen, K. H., Korkeila, M., Bogl, L. H., Westerterp, K. R., Yki-Järvinen, H., Kaprio, J., & Rissanen, A. (2010). Inaccuracies in food and physical activity diaries of obese subjects: Complementary evidence from doubly labeled water and co-twin assessments. *International Journal of Obesity*, 34, 437–445.
- Rizzuto, D., & Fratiglioni, L. (2014). Lifestyle factors related to mortality and survival: A mini-review. *Gerontology*, 60, 327–335.
- Skytthe, A., Kyvik, K., Bathum, L., Vaupel, J. W., & Christensen, K. (2006). The Danish twin registry in the new millennium. *Twin Research and Human Genetics*, 9, 763–771.
- Skytthe, A., Kyvik, K., Holm, N. V., Vaupel, J. W., & Christensen, K. (2002). The Danish twin registry: 127 cohorts of twins. *Twin Research and Human Genetics*, 5, 352–357.
- Taylor, D. (2014). Physical activity is medicine for older adults. *Postgraduate Medical Journal*, 90, 26–32.
- Thinggaard, M., Jacobsen, R., Jeune, B., Martinussen, T., & Christensen, K. (2010). Is the relationship between BMI and mortality increasingly U-shaped with advancing age? A 10-year follow-up of persons aged 70–95 years. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 65, 526–531.
- Thygesen, L. C., & Ersbøll, A. K. (2011). Danish population-based registers for public health and health-related welfare research: Introduction to the supplement. *Scandinavian Journal of Public Health*, 29, 8–10.
- Tomassini, C., Juel, K., Holm, N. V., Skytthe, A., & Christensen, K. (2003). Risk of suicide in twins: 51-year follow-up study. *British Medical Journal*, 327, 373–374.
- Torres, S. J., & Nowson, C. A. (2007). Relationship between stress, eating behavior, and obesity. *Nutrition*, 23, 887–894.
- Vogel, T., Brechat, P.-H., Leprêtre, P.-M., Kaltenbach, G., Berthel, M., & Lonsdorfer, J. (2009). Health benefits of physical activity in older patients: A review. *International Journal of Clinical Practice*, 63, 303–320.
- Warburton, D. E. R., Nicol, C. W. N., & Bredin, S. S. D. (2006). Health benefits of physical activity: The evidence. *Canadian Medical Association Journal*, 174, 801–809.
- Westerterp, K. R. (2010). Physical activity, food intake, and body weight regulation: Insights from doubly labeled water studies. *Nutrition Reviews*, 68, 148–154.